FILE 'BIOSIS' ENTERED AT 10:13:03 ON 16 AUG 2002 COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

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FILE 'EMBASE' ENTERED AT 10:13:03 ON 16 AUG 2002 COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

=> s oxbutyrate

L1 0 OXBUTYRATE

=> s oxobutyrate and plant

L2 54 OXOBUTYRATE AND PLANT

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- L3 ANSWER 1 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 2002:232069 BIOSIS
- DN PREV200200232069
- TI Characterization of the aromatic profile in aqueous essence and fruit juice of yellow passion fruit (Passiflora edulis Sims F. Flavicarpa degner) by GC-MS and GC/O.
- AU Jordan, Maria J.; Goodner, Kevin L. (1); Shaw, Philip E.
- CS (1) Citrus and Subtropical Products Laboratory, U.S. Department of Agriculture, 600 Avenue S, N.W., Winter Haven, FL, 33881: goodner@citrus.usda.qov USA
- Journal of Agricultural and Food Chemistry, (March 13, 2002) Vol. 50, No. 6, pp. 1523-1528. http://pubs.acs.org/journals/jafcau. print. ISSN: 0021-8561.
- DT Article
- LA English
- L3 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2002 ACS
- AN 2001:624164 CAPLUS
- DN 135:195498
- TI Preparation of indole derivatives
- IN Yokoyama, Mineyuki; Yamaguchi, Shoko; Iida, Toshiyuki; Kobayashi, Koji
- PA Shiseido Co., Ltd., Japan
- SO Jpn. Kokai Tokkyo Koho, 7 pp.
- CODEN: JKXXAF
- DT Patent
- LA Japanese
- FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

- PI JP 2001233856 A2 20010828 JP 2000-47141 20000224
- OS CASREACT 135:195498; MARPAT 135:195498
- L3 ANSWER 3 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
- AN 2001:473120 BIOSIS

- DN PREV200100473120
- TI 1-Aminocyclopropane-1-carboxylate synthase of Penicillium citrinum: Primary structure and expression in Escherichia coli and Saccharomyces cerevisiae.
- AU Kakuta, Yukiko; Igarashi, Toshinori; Murakami, Toyotaka; Ito, Hiroyuki; Matsui, Hirokazu (1); Honma, Mamoru
- CS (1) Graduate School of Agriculture, Hokkaido University, Sapporo, 060-8589: mhiro@chem.agr.hokudai.ac.jp Japan
- SO Bioscience Biotechnology and Biochemistry, (July, 2001) Vol. 65, No. 7, pp. 1511-1518. print. ISSN: 0916-8451.
- DT Article
- LA English
- SL English
- L3 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2002 ACS
- AN 2000:658481 CAPLUS
- DN 133:238025
- TI Preparation of azinyl phenyl ethers as herbicides and plant desiccants.
- IN Pulman, David A.; Ying, Bai-Ping; Wu, Shao-Yong; Gupta, Sandeep;
 Tsukamoto, Masamitsu; Haga, Takahiro
- PA Ishihara Sangyo Kaisha, Ltd., Japan
- SO U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 151,306. CODEN: USXXAM
- DT Patent
- LA English
- FAN.CNT 1

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os	MARPAT 133:23802	5			

- RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L3 ANSWER 5 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
- AN 2000:240951 BIOSIS
- DN PREV200000240951
- TI 1-aminocyclopropane-1-carboxylate (ACC) deaminase induced by ACC synthesized and accumulated in Penicillium citrinum intracellular spaces.
- AU Jia, Yan-Jun (1); Ito, Hiroyuki; Matsui, Hirokazu; Honma, Mamoru
- CS (1) Graduate School of Agriculture, Hokkaido University, Sapporo, 060-8589

 Japan
- SO Bioscience Biotechnology and Biochemistry, (Feb., 2000) Vol. 64, No. 2, pp. 299-305.
 ISSN: 0916-8451.
- DT Article
- LA English
- SL English
- L3 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2002 ACS
- AN 1999:35006 CAPLUS
- DN 130:106028
- TI Use of DNA encoding plastid pyruvate dehydrogenase and branched chain oxoacid dehydrogenase components to enhance polyhydroxyalkanoate biosynthesis in **plants**
- IN Randall, Douglas R.; Johnston, Mark L.; Miernyk, Jan A.; Luethy, Michael H.; Mooney, Brian P.
- PA University of Missouri, USA
- SO PCT Int. Appl., 151 pp.

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             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
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     US 1998-76544P P 19980302
     US 1998-76554P
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     WO 1998-US13406 W
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              THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
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     ANSWER 7 OF 37 CAPLUS COPYRIGHT 2002 ACS
     1999:409262 CAPLUS
AN
DN
     131:87918
     Preparation of azole derivatives as herbicides
ΤI
     Sato, Kazuo; Sano, Hiroki; Komai, Hiroyuki; Kudo, Noriaki; Morimoto,
IN
     Munetsugu; Kadotani, Junji
PA
     Sankyo Co., Ltd., Japan
     Jpn. Kokai Tokkyo Koho, 84 pp.
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     Japanese
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     MARPAT 131:87918
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     ANSWER 8 OF 37 AGRICOLA
                                                       DUPLICATE 3
ΑN
     2000:14113 AGRICOLA
DN
     IND22022414
     Physiological consequences of mutation for ALS-inhibitor resistance.
TI
     Eberlein, C.V.; Guttieri, M.J.; Berger, P.H.; Fellman, J.K.;
AU
     Mallory-Smith, C.A.; Thill, D.C.; Baerg, R.J.; Belknap, W.R. University of Idaho, Twin Falls.
CS
ΑV
     DNAL (79.8 W41)
SO
     Weed science, July/Aug 1999. Vol. 47, No. 4. p. 383-392
     Publisher: Lawrence, KS: Weed Science Society of America.
     CODEN: WEESA6; ISSN: 0043-1745
NTE
     Includes references
     Kansas; United States
CY
DT
     Article
FS
     U.S. Imprints not USDA, Experiment or Extension
LA
     English
L_3
     ANSWER 9 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN
     1999:450939 BIOSIS
DN
     PREV199900450939
     Synthesis, characterization and antimicrobial evaluation of ethyl
TI
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CODEN: PIXXD2

2-arylhydrazono-3-oxobutyrates. ΑU Kucukguzel, S. Guniz; Rollas, Sevim (1); Erdeniz, Habibe; Kiraz, Muammer (1) Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Marmara CS University, Tibbiye cad. 81010, Haydarpasa, Istanbul Turkey European Journal of Medicinal Chemistry, (Feb., 1999) Vol. 34, No. 2, pp. SO 153-160. ISSN: 0223-5234. Article DTLA English English ŞL L3 ANSWER 10 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. AN 1999:247306 BIOSIS PREV199900247306 DN TI Reduction of beta-keto esters with a reductase: Construction of plural stereocenters remote from the reaction center. ΑU Kawai, Yasushi (1); Hida, Kouichi; Ohno, Atsuyoshi (1) Institute for Chemical Research, Kyoto University, Uji, Kyoto, CS 611-0011 Japan SO Bioorganic Chemistry, (Feb., 1999) Vol. 27, No. 1, pp. 3-19. ISSN: 0045-2068. DT Article LA English SL English => s 13 and 2-oxobutyrate 16 L3 AND 2-OXOBUTYRATE => d l4 1-16 L4ANSWER 1 OF 16 AGRICOLA AN 2000:14113 AGRICOLA DN IND22022414 TIPhysiological consequences of mutation for ALS-inhibitor resistance. ΑU Eberlein, C.V.; Guttieri, M.J.; Berger, P.H.; Fellman, J.K.; Mallory-Smith, C.A.; Thill, D.C.; Baerg, R.J.; Belknap, W.R. University of Idaho, Twin Falls. CS ΑV DNAL (79.8 W41) SO Weed science, July/Aug 1999. Vol. 47, No. 4. p. 383-392 Publisher: Lawrence, KS: Weed Science Society of America. CODEN: WEESA6; ISSN: 0043-1745 NTE Includes references Kansas; United States CYDTArticle FS U.S. Imprints not USDA, Experiment or Extension LAEnglish ANSWER 2 OF 16 AGRICOLA L41999:15022 AGRICOLA ANDNIND21965730 ΤI Biosynthesis of 2-aceto-2-hydroxy acids: acetolactate synthases and acetohydroxyacid synthases. ΑU Chipman, D.; Barak, Z.; Schloss, J.V. CS Ben Gurion University of the Negev, Beer Sheva, Israel. ΑV DNAL (381 B522) Biochimica et biophysica acta = International journal of biochemistry and SO biophysics, June 29, 1998. Vol. 1385, No. 2. p. 401-419 Publisher: Amsterdam : Elsevier Science B.V. CODEN: BBACAO; ISSN: 0006-3002 NTEIncludes references CY Netherlands DTArticle; Law FS Non-U.S. Imprint other than FAO

- LA English
- L4 ANSWER 3 OF 16 AGRICOLA
- AN 95:32822 AGRICOLA
- DN IND20460545
- TI Repression of acetolactate synthase activity through antisense inhibition.
- AU Hofgen, R.; Laber, B.; Schuttke, I.; Klonus, A.K.; Streber, W.; Pohlenz,
- CS Max-Planck-Institut fur Molekulare Pflanzenphysiologie, Potsdam, Germany.
- AV DNAL (450 P692)
- SO Plant physiology, Feb 1995. Vol. 107, No. 2. p. 469-477
 Publisher: Rockville, MD: American Society of Plant Physiologists, 1926CODEN: PLPHAY; ISSN: 0032-0889
- NTE Includes references
- CY Maryland; United States
- DT Article; Conference
- FS U.S. Imprints not USDA, Experiment or Extension
- LA English
- L4 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 2001:473120 BIOSIS
- DN PREV200100473120
- TI 1-Aminocyclopropane-1-carboxylate synthase of Penicillium citrinum: Primary structure and expression in Escherichia coli and Saccharomyces cerevisiae.
- AU Kakuta, Yukiko; Igarashi, Toshinori; Murakami, Toyotaka; Ito, Hiroyuki; Matsui, Hirokazu (1); Honma, Mamoru
- CS (1) Graduate School of Agriculture, Hokkaido University, Sapporo, 060-8589: mhiro@chem.agr.hokudai.ac.jp Japan
- SO Bioscience Biotechnology and Biochemistry, (July, 2001) Vol. 65, No. 7, pp. 1511-1518. print. ISSN: 0916-8451.
- DT Article
- LA English
- SL English
- L4 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 2000:240951 BIOSIS
- DN PREV200000240951
- TI 1-aminocyclopropane-1-carboxylate (ACC) deaminase induced by ACC synthesized and accumulated in Penicillium citrinum intracellular spaces.
- AU Jia, Yan-Jun (1); Ito, Hiroyuki; Matsui, Hirokazu; Honma, Mamoru
- CS (1) Graduate School of Agriculture, Hokkaido University, Sapporo, 060-8589 Japan
- SO Bioscience Biotechnology and Biochemistry, (Feb., 2000) Vol. 64, No. 2, pp. 299-305.
 ISSN: 0916-8451.
- DT Article
- LA English
- SL English
- L4 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 1998:126857 BIOSIS
- DN PREV199800126857
- TI Identification and stereospecificity of the first three enzymes of 3-dimethylsulfoniopropionate biosynthesis in a chlorophyte alga.
- AU Summers, Peter S.; Nolte, Kurt D.; Cooper, Arthur J. L.; Borgeas, Heidi; Leustek, Thomas; Rhodes, David; Hanson, Andrew D. (1)
- CS (1) Horticultural Sci. Dep., Univ. Florida, Gainesville, FL 32611 USA
- SO Plant Physiology (Rockville), (Jan., 1998) Vol. 116, No. 1, pp. 369-378. ISSN: 0032-0889.
- DT Article
- LA English

- ANSWER 7 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L4
- 1998:84107 BIOSIS AΝ
- PREV199800084107 DN
- S-methylmethionine conversion to dimethylsulfoniopropionate: Evidence for TTan unusual transamination reaction.
- Rhodes, David; Gage, Douglas A.; Cooper, Arthur J. L.; Hanson, Andrew D. ΑU
- (1) Horticultural Sci. Dep., Univ. Florida, Gainesville, FL 32611 USA CS
- Plant Physiology (Rockville), (Dec., 1997) Vol. 115, No. 4, pp. 1541-1548. SO ISSN: 0032-0889.
- DT Article
- English LA
- ANSWER 8 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L4
- 1990:266122 BIOSIS AN
- BA90:8208 DN
- DIHYDRODIPICOLINATE SYNTHASE OF NICOTIANA-SYLVESTRIS A TICHLOROPLAST-LOCALIZED ENZYME OF THE LYSINE PATHWAY.
- ΑU GHISLAIN M; FRANKARD V; JACOBS M
- LAB. PLANT GENETICS, VRIJE UNIV. BRUSSEL, PAARDENSTR. 65, B-1640 CS ST.-GENESIUS RODE, BELGIUM.
- PLANTA (HEIDELB), (1990) 180 (4), 480-486. so CODEN: PLANAB. ISSN: 0032-0935.
- FS BA; OLD
- English LΑ
- ANSWER 9 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L4
- 1988:291804 BIOSIS AN
- DNBA86:20071
- STEREOSELECTIVITY OF THE INTERACTION OF E-2 PHOSPHOENOLBUTYRATE AND Z-2 TIPHOSPHOENOLBUTYRATE WITH MAIZE LEAF PHOSPHOENOLPYRUVATE CARBOXYLASE.
- GONZALEZ D H; ANDREO C S ΑU
- CENTRO ESTUDIOS FOTOSINTETICOS BIOQUIMICOS, UNIV. NAC. ROSARIO, SUIPACHA CS 531, RA-2000 ROSARIO, ARGENT.
- EUR J BIOCHEM, (1988) 173 (2), 339-344. SO CODEN: EJBCAI. ISSN: 0014-2956.
- FS BA; OLD
- LAEnglish
- ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. T.4
- AN 1987:446393 BIOSIS
- DN BA84:102231
- TIAMINO ACID METABOLISM OF LEMNA-MINOR L. II. RESPONSES TO CHLORSULFURON.
- RHODES D; HOGAN A L; DEAL L; JAMIESON G C; HAWORTH P ΑU
- DEP. HORTICULTURE, PURDUE UNIV., WEST LAFAYETTE, INDIANA 47907. PLANT PHYSIOL (BETHESDA), (1987) 84 (3), 775-780. CS
- SO CODEN: PLPHAY. ISSN: 0032-0889.
- FS BA; OLD
- LA English
- ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS L4
- 2000:658481 CAPLUS AN
- DN 133:238025
- Preparation of azinyl phenyl ethers as herbicides and plant ΤI desiccants.
- Pulman, David A.; Ying, Bai-Ping; Wu, Shao-Yong; Gupta, Sandeep; ΙN Tsukamoto, Masamitsu; Haga, Takahiro
- PΑ Ishihara Sangyo Kaisha, Ltd., Japan
- U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 151,306. SO CODEN: USXXAM
- DTPatent
- English LA
- FAN.CNT 1
 - PATENT NO. KIND DATE

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US 1998-159233
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    US 6121201 A
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     1999:35006 CAPLUS
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     130:106028
DN
     Use of DNA encoding plastid pyruvate dehydrogenase and branched chain
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     oxoacid dehydrogenase components to enhance polyhydroxyalkanoate
     biosynthesis in plants
     Randall, Douglas R.; Johnston, Mark L.; Miernyk, Jan A.; Luethy, Michael
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     H.; Mooney, Brian P.
     University of Missouri, USA
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     PCT Int. Appl., 151 pp.
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     ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
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AN
     1997:425802 CAPLUS
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     127:173598
     A new route for synthesis of dimethylsulfoniopropionate in marine algae
ΤI
     Gage, Douglas A.; Rhodes, David; Nolte, Kurt D.; Hicks, Wayne A.; Leustek,
AU
     Thomas; Cooper, Arthur J. L.; Hanson, Andrew D.
     Dep. Biochem., Michigan State Univ., East Lansing, MI, 48824, USA
CS
     Nature (London) (1997), 387(6636), 891-894
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     CODEN: NATUAS; ISSN: 0028-0836
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     Journal
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     English
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     ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN
     1990:232557 CAPLUS
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     112:232557
ΤI
     Modified branched-chain amino acid pathways give rise to acyl acids of
     sucrose esters exuded from tobacco leaf trichomes
ΑU
     Kandra, Lili; Severson, Ray; Wagner, George Joseph
CS
     Agron. Dep., Univ. Kentucky, Lexington, KY, 40546-0091, USA
     Eur. J. Biochem. (1990), 188(2), 385-91
SO
     CODEN: EJBCAI; ISSN: 0014-2956
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     1988:470470 CAPLUS
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     Amino acid metabolism of Lemna minor L. III. Responses to
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ΑU
     Brunk, Dennis G.; Rhodes, David
CS
     Cent. Plant Environ. Stress Physiol., Purdue Univ., West Lafayette, IN,
     47907, USA
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     Plant Physiol. (1988), 87(2), 447-53
     CODEN: PLPHAY; ISSN: 0032-0889
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LA
     English
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KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
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L7 ANSWER 1 OF 24 AGRICOLA

L7 ANSWER 2 OF 24 AGRICOLA

Levels of expression of two subunits of the liver branched-chain alpha-AΒ ketoacid dehydrogenase complex in response to extremes of dietary protein intake (50% versus 0% protein diet) were determined by quantitative immunoblotting. Dietary protein deficiency decreased the amount of **E1** alpha protein to a greater extent than E2 protein. The ratio of E1 alpha to E2 was below 1 in the liver of animals starved for protein and above 1 in the liver of animals fed the high-protein diet. Supplementation of the 0% protein diet with 5% leucine (but not 5% valine) had the same effect as the 50% protein diet. The extremes of dietary protein also resulted in a divergent pattern of expression of the mRNAs for the subunits of the complex. The **E1** beta message showed the expected corollary of being greater in the liver of the high-protein-fed rats than the no-protein-fed rats. In contrast, the E2 message was not affected by the two extremes of dietary protein and the E1 alpha message was greater in the liver of the no-protein-fed rats than the high-protein-fed rats. Thus, coordinate regulation of gene expression of the subunits of the complex does not occur in response to dietary protein. Post-transcriptional regulatory mechanisms most likely determine the amount of the complex and the ratio of its subunits. The decrease in E1 alpha/E2 protein ratio that occurs in dietary protein deficiency may increase sensitivity of the complex to phosphorylationmediated inhibition by branched-chain alpha-ketoacid dehydrogenase kinase.

1.7 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. The branched-chain alpha-ketoacid dehydrogenase (BCKDH) complex is the AB rate-limiting enzyme in the catabolism of branched-chain amino acids. In the present study, we examined the effects of exercise training on the activity and enzyme expression of the hepatic BCKDH complex in diabetic rats. The rats were prepared by intravenous injections of streptozotocin (50 mg/kg BW), and exercise training was accomplished by treadmill running for 45 min/d for 4 wk. The total and actual activities of hepatic BCKDH complex were significantly increased to apprx160% by 4 wk of diabetes. On the other hand, diabetic rats in the trained group had the same level of activities as those in the normal rats, indicating that exercise training inhibited the diabetes-induced increase in the enzyme activities. The activity state (% active form) of the enzyme complex was about 100% in all groups and was not affected by diabetes or training. The protein amounts of the enzyme subunits (Elalpha and E2) and the abundance of mRNA for the E2 subunit, but not for the other subunits, in the liver had the same trend as the activities. These results suggest that the capacity for branched-chain amino acid catabolism in streptozotocin-induced diabetic rats is reduced by exercise training and

that this modification is associated with the suppression of diabetes-induced BCKDH complex expression in the liver.

- ANSWER 4 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7 Untreated maple syrup urine disease (MSUD) results in mental and physical AB disabilities and often leads to neonatal death. Newborn-screening programs, coupled with the use of protein-modified diets, have minimized the severity of this phenotype and allowed affected individuals to develop into productive adults. Although inheritance of MSUD adheres to rules for single-gene traits, mutations in the genes for Elalpha, Elbeta, or E2 of the mitochondrial branched-chain alphaketoacid dehydrogenase complex can cause the disease. Randomly selected cell lines from 63 individuals with clinically diagnosed MSUD were tested by retroviral complementation of branched-chain alpha-ketoacid dehydrogenase activity to identify the gene locus for mutant alleles. The frequencies of the mutations were 33% for the Elalpha gene, 38% for the Elbeta gene, and 19% for the E2 gene. Ten percent of the tested cell lines gave ambiguous results by showing no complementation or restoration of activity with two gene products. These results provide a means to establish a genotype/phenotype relationship in MSUD, with the ultimate goal of unraveling the complexity of this single-gene trait. This represents the largest study to date providing information on the genotype for MSUD.
- ANSWER 5 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. 1.7 AΒ A family of alpha -ketoacid dehydrogenase complex includes alpha -ketoglutarate dehydrogenase (alpha -KGDC), pyruvate dehydrogenase and branched chain alpha -ketoacid dehydrogenase complexes. These three complexes are composed of three different component enzymes, alpha -ketoacid decarboxylase (E1), dihydrolipoamide acyltransferase (E2) and dihydrolipoamide dehydrogenase (E3). We isolated and sequenced cDNA clones for the dihydrolipoamide succinyltransferase (E2 of alpha -KGDC, designated as DLST) components of the rat and human alpha -KGDCs. The primary structures of the rat and human DLSTs showed close similarity to those of E. coli and A. vinelandii DLSTs. However, the rat and human DLSTs did not contain a sequence motif that had been found as an E3 and/or El binding domain in the E2 components of three alpha ketoacid dehydrogenase complexes, suggesting the lack of the E3 and/or E1 binding domain in the rat and human DLSTs. The result of phylogenetic tree of the E2 components of three complexes demonstrated that the lack of the domain in rat and human DLSTs might occur after the mitochondrial symbiosis. Next, we isolated genomic DNA and processed pseudogene of human DLST and determined their entire nucleotide sequences. In situ hybridization analysis demonstrated that the human DLST gene is located on chromosome 14 at q24.2-q24.3 and the pseudogene is located on chromosome 1 at p31. The results of CAT and gel shift assays showed that another protein rather than Sp1 plays a significant role with Ap2 in the transcription - regulation of DLST gene. In addition, we detected polymorphisms in the human DLST gene and found an association of a genotype (ac/ac type) of DLST gene with Alzheimer's disease. Furthermore, we have observed that in the skeletal muscle the ${\tt DLST}$ is also localized on the plasma membrane and sarcoplasmic reticulum and that the molecule (25 kDa) is smaller than mitochondrial DLST (48
- L7 ANSWER 6 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

 AB Regulation of the mammalian branched-chain alpha-ketoacid

 dehydrogenase complex (BCKAD) occurs under a variety of

 stressful conditions associated with changes in circulating

 glucocorticoids. Multiple levels of regulation in hepatocytes, including

 alteration of the levels of the structural subunits available for assembly

 (E1, alpha-ketoacid decarboxylase; E2,

 dihydrolipoamide acyltransferase; and E3, dihydrolipoamide dehydrogenase),

kDa).

as well as BCKAD kinase, which serves to phosphorylate the Elalpha subunit and inactivate complex activity, have been proposed. The direct role of glucocorticoids in regulating the expression of the murine gene encoding the major BCKAD subunit E2, upon which the other BCKAD subunits assemble, was therefore examined. Deletion analysis of the 5' proximal 7.0 kb of the murine E2 promoter sequence, using E2 promoter/luciferase expression minigene plasmids introduced into the hepatic H4IIEC3 cell line, suggested a promoter proximal region responsive to glucocorticoid regulation. Linker-scanning mutagenesis combined with deletion analysis established this functional glucocorticoid-responsive unit (GRU) to be located near the murine **E2** proximal promoter site at -140 to -70 bp upstream from the transcription initiation site. The presence of this region in plasmid minigenes, containing varying amounts of the murine genomic sequence 5' upstream from proximal E2 promoter sequences, conferred 2-10 fold increases in luciferase reporter gene expression in H4IIEC3 cells, whether introduced by transient transfection or following co-selection for stable transfectants. The GRU region itself appeared to contain multiple interacting elements that combine to regulate overall E2 promoter activity in response to changing physiological conditions associated with varying concentrations of glucocorticoids and likely other hormonal effectors.

- ANSWER 7 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7Maple syrup urine disease (MSUD) was first described in 1954 by Menkes et AB al. as a progressive neurologic degenerative disorder. In 1960, Dancis et al. established that the metabolic block in MSUD is at the decarboxylation of branched-chain alpha-ketoacids derived from leucine, isoleucine, and valine. The multienzyme complex affected in MSUD, the mitochondrial branched-chain alpha-ketoacid (BCKD) dehydrogenase complex was purified in 1978 to homogeneity in Reed's laboratory. This led to the later cloning of cDNAs and genes for subunits of the human BCKD complex. Genetic heterogeneity in MSUD is now explained by the various mutations that occur in the Elalpha, Elbeta, E2, and E3 loci of the BCKD complex. Recently, we found that bacterial chaperonins GroEL and GroES promote folding and assembly of E1 decarboxylase component of the BCKD complex in Escherichia coli. Pulse-chase labeling in this system showed that a subset of Elalpha mutations, notably the homozygous Y393N-alpha in Mennonite MSUD patients, impedes the assembly of the mutant Elalpha subunit with normal Elbeta. The assembly defect is associated with a rapid degradation of the normal Elbeta subunit in MSUD cells. Retrovirus-mediated transduction of lymphoblasts from a Mennonite MSUD patient with a normal Elalpha cDNA resulted in a complete restoration of BCKD activity. This was accompanied by a stabilization of the normal Elbeta subunit through assembly with recombinant Elalpha. The results demonstrated the feasibility of stable correction of Elalpha -deficient (type IA) MSUD and provided a basis for the development of gene therapy.
- L7 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- L7 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AB Regulation of the branched chain alpha-ketoacid
 dehydrogenase complex, the rate-limiting enzyme of
 branched chain amino acid catabolism, involves phosphorylation of 2 amino
 acid residues (site 1, serine 293; site 2, serine 303). To directly assess
 the roles played by these sites, site-directed mutagenesis was used to
 convert these serines to glutamates and/or alanines. Functional E1
 heterotetramers were expressed in Escherichia coli carrying genes for
 E1-alpha and E1-beta under control of separate T7
 promoters in a dicistronic vector. Mutation of phosphorylation site 1
 serine to glutamate inactivated E1 activity, i.e., mimicked the
 effect of phosphorylation of site 1. Replacement of the site 1 serine with

alanine greatly increased K-m for the alpha-ketoacid substrate but had no effect on maximum velocity. The site 1 serine to alanine mutant was phosphorylated at site 2, but phosphorylation had no effect upon enzyme activity. Mutation of site 2 serine to either glutamate or alanine also had no effect upon enzyme activity, but phosphorylation of these proteins at site 1 inhibited enzyme activity. E1 mutated to change both phosphorylation site serines to glutamates was without enzyme activity. The binding affinity of E1 to the E2 core was not affected by mutation of the phosphorylation sites to glutamates, suggesting no gross perturbation of the association of E1 with the E2 core. The results provide direct evidence that a negative charge at phosphorylation site 1 is responsible for kinase-mediated inactivation of E1. Site 2 is silent with respect to regulation of activity by phosphorylation.

ANSWER 10 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. 1.7 The response of the murine genes encoding the subunits of branched-chain AΒ alpha-ketoacid dehydrogenase complex (BCKAD) to changes in dietary protein was determined. Steady-state RNA levels for two of the subunits, E1-beta and E2, decreased by twoto fourfold in the livers of mice fed 0% protein isocaloric diets compared to the levels observed in mice fed standard (23 %) or high (50 %) protein isocaloric diets. In contrast, the levels of RNA encoding the E1 -alpha subunit did not change significantly in response to these dietary protein changes. The hepatic decreases in E1-beta and E2 RNA associated with 0% protein isocaloric diets were reversible, with prompt return to baseline levels following 48 hours of 50% protein isocaloric diets ad libitum. In kidney, no significant changes in the RNAs encoding any of the three BCKAD subunits were observed in response to changes in dietary protein. Studies of RNA variations associated with growth and development in several murine tissues, including liver and kidney, demonstrated coordinated changes between all subunits. Similar coordinated changes were observed during 3T3-L1 adipocyte differentiation. These studies suggest that the responses of the BCKAD subunit genes to alterations in dietary protein are noncoordinated and tissue-specific, in contrast to the coordinated changes observed during growth and/or differentiation. The differences in BCKAD subunit RNA levels observed under varying nutritional and developmental conditions suggest that multiple regulatory mechanisms modulate BCKAD subunit expression.

ANSWER 11 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7AB Anti-M2 antibodies in primary biliary cirrhosis (PBC) have been shown to react with the alpha-ketoacid dehydrogenase complex of the inner mitochondrial membrane consisting of six epitopes (E2 subunit of the pyruvate dehydrogenase complex (PDC), 70 kD: protein X of the PDC, 56 kD; alpha-ketoglutarate dehydrogenase complex, 52 kD; branched-chain alpha-ketoacid dehydrogenase, 52 kD; E1 alpha subunit of PDC, 45 kD; and E1 beta-subunit of PDC, 36 kD). These epitopes are also present in the M2 fraction which is a chloroform extract from beef heart mitochondria. The E2 subunit of the PDC at 70 kD (M2a), especially, is a major target epitope which is recognized by about 85% of all PBC sera. However, analysing sera from 28 patients with active pulmonary tuberculosis it became evident that 12 (43%) also recognized the PDC-E2 subunit (M2a), as shown by Western blotting using the M2 fraction, the purified PDC, and the recombinant PDC-E2. In contrast, only two of 82 patients with other bacterial and viral infections including 25 patients with Escherichia coli infections reacted with the PBC-specific epitope at 70 kD. Naturally occurring mitochondrial antibodies (NOMA) were present in 54% of the patients with tuberculosis and in 50% of patients with other infectious disorders. They recognized either a determinant at 65 kD (epsilon) or at 60/55 kD (zeta/eta). None of the sera from 100 blood donors had anti-M2 but 14 had NOMA. Testing anti-M2 and NOMA-positive marker sera by Western blotting against membrane fractions derived from

mycobacteria and E. coli it could be shown that sbd like mammalian mitochondria sbd they contain both the PBC-specific M2 antigen as well as the non-PBC-specific naturally occurring mitochondrial antigen system (NOMAg). The observation that PBC-specific antibodies were preferentially induced in patients suffering from a mycobacterial infection may provide some new clues to the still unknown etiology of PBC.

- ANSWER 12 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7 We have expressed an active recombinant E1 decarboxylase AΒ component of the mammalian branched-chain .alpha.-ketoacid dehydrogenase complex in Escherichia coli by subcloning mature E1.alpha. and E1.beta. subunit cDNA sequences into a bacterial expression vector. To permit affinity purification under native conditions, the mature E1.alpha. subunit was fused with affinity ligand E. coli maltose-binding protein (MBP) through an endoprotease Factor Xa-specific linker peptide. When coexpressed, the MBP-E1.alpha. fusion and E1.beta. subunits were shown to co-purify as a MBP-E1 component that exhibited both E1 activity and binding competence for recombinant branched-chain E2 component. In contrast, in vitro mixing of individually expressed MBP-E1.alpha. and E1.beta. did not result in assembly or produce E1 activity. Following proteolytic removal of the affinity ligand and linker peptide with Factor Xa, a recombinant E1 species was eluted from a Sephacryl S-300HR sizing column as an enymatically active 160-kDa species. The latter showed 1:1 subunit stoichiometry, which was consistent with a .alpha.2.beta.2 structure. The recovery of this 160-kDa recombiinant E1 species (estimated at 0.07% of total lysate protein) was low, with the majority of the recombinant protein lost as insoluble aggregates. Our findings suggest that the concurrent expression of both E1.alpha. and E1 .beta. subunits in the same cellular compartment is important for assembly of both subunits into a functional E1 .alpha.2.beta.2 heterotetramer. By using this co-expression system, we also find that the E1.alpha. missense mutation (Tyr-393 .fwdarw. Asn) characterized in Mennonites with maple syrup urine disease prevents the assembly of soluble E1 heterotetramers.
- ANSWER 13 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7 Maple syrup urine disease (MSUD) is an autosomal recessive inherited AB disease due to a deficiency of any of the subunits, E1.alpha., E1.beta., or E2, of the branched-chain .alpha.ketoacid dehydrogenase complex (BCKDH). A large Mennonite kindred of MSUD has been studied in Pennsylvania, USA. In the present investigation, genomes from 70 members, including 12 patients belonging to eight different Mennonite MSUD pedigrees, were examined for possible abnormalities in the E1.alpha. gene of BCKDH, by primer-specified restriction map modification. A T- to -A substitution which generates an asparagine in place of a -tyrosine at amino acid 394 of the mature **E1**.alpha. subunit was present in both alleles in all the patients and in a single allel in all obligate carriers and several siblings. We describe a new technique for rapid for an easy detection of the mutant gene in this population. These family studies provide additional evidence that Mennonite MSUD is caused by a missense mutation of the E1.alpha. gene of BCKDH.
- ANSWER 14 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

 A complementary DNA (cDNA) clone of dihydrolipoamide acetyltransferase (
 E2) of the rat pyruvate dehydrogenase complex (PDC) was isolated from a .lambda.gt11 rat heart cDNA library. The amino acid sequence of a full mature protein of rat PDC-E2 was predicted by combination of the cDNA nucleotide sequence and the N-terminal amino acid sequence determined chemically. The amino acid sequence of rat PDC-E2 was well consistent with those of the E2 components of other .alpha.-ketoacid dehydrogenase complexes.

These E2 components possess the sequence G-X-G-X-X-G, which is the consensus sequence for nucleotide binding sites of nucleotide binding proteins, in the E3 and/or E1 binding domains. The E2 components of the three .alpha.-ketoacid dehydrogenase complexes are suggested to be classified into three clusters separated during evolution.

- L7 ANSWER 15 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- Answer 16 of 24 biosis copyright 2002 biological abstracts inc.

 Antibodies against the **Elb** and **E2b** components of bovine branched-chain .alpha.-ketoacid (BCKA) dehydrogenase (BCKAD) complex completely inhibited BCKA oxidation in mammalian and avian mitochondria. BCKA oxidation by salmonid mitochondria was less affected and the enzyme from Pseudomonas putida was unaffected. In rodents, anti-**E1b E2b** IgG inhibited oxidation of all three BCKA in a similar dose-dependent manner; oxidation of .alpha.-ketobutyrate and .alpha.-keto-.gamma.-methiolbutyrate was also partially inhibited. Except for the salmonid BCKAD, a similar Mr for the **E2b** and **E1b** .alpha. proteins was observed in these species. After digestion with V-8 protease similar immunoreactive peptides were observed for the human and rodent complex.
- ANSWER 17 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7The native architectures of the pyruvate and 2-oxoglutarate dehydrogenase AB complexes have been investigated cryoelectron microscopy of unstained, frozen-hydrated specimens. In pyruvate dehydrogenase complex and 2-oxoglutarate complex the transacylase (E2) components exist as 24-subunit, cube-shaped assemblies that form the structural cores of the complexes. Multiple copies (12-24) of the .alpha.-ketoacid dehydrogenase (E1) and dihydrolipoyl dehydrogenase (E3) components bind to the surface of the cores. Images of the frozen-hydrated enzyme complexes do not appear consistent with a symmetric arrangement of the E1 and E3 subunits about the octahedrally symmetric E2 core. Often the E1 or E3 subunits appear separated from the surface of the E2 core by 3-5 nm, and sometimes thin bridges of density appear in the gap between the E2 core and the bound subunits; studies of subcomplexes consisting of the E2 core from 2-oxoglutarate dehydrogenase complex and E1 or E3 show that both E1 and E3 are bound in this manner. Images of the E2 cores isolated from pyruvate dehydrogenase complex appear surrounded by a faint fuzz that extends .apprx. 10 nm from the surface of the core and likely corresponds to the lipoyl domains of the E2.
- ANSWER 18 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7Sera from patients with primary biliary cirrhosis contain autoantibodies AΒ that recognize mitochondrial proteins. Five of the target autoantigens have now been identified as enzymes of three related multienzyme complexes: the pyruvate dehydrogenase complex, the branched chain .alpha.ketoacid dehydrogenase complex and the .alpha.-ketoglutarate dehydrogenase complex. Each complex consists of component enzymes designated E1, E2 and E3. In this report, we confirm that primary biliary cirrhosis sera react with dihydrolipoamide succinyltransferase, the E2 component of .alpha.-ketoglutarate dehydrogenase complex. Seventy-three of 188 (39%) primary biliary cirrhosis sera reacted with .alpha.-ketoglutarate dehydrogenase complex-E2 when immunoblotted against purified .alpha.-ketoglutarate dehydrogenase complex; one of these sera also reacted with the E1 component. In addition, primary biliary cirrhosis sera possessing .alpha.-ketoglutarate dehydrogenase complex-E2 reactivity specifically inhibited enzyme function of .alpha.-ketoglutarate dehydrogenase complex. Enzyme activity was not affected by primary biliary cirrhosis sera that contained autoantibodies to pyruvate dehydrogenase complex-E2 and/or branched chain

.alpha.-ketoacid dehydrogenase comples-E2, which lacked .alpha.-ketoglutarate dehydrogenase complex-E2 reactivity. Furthermore, affinity-purified primary biliary cirrhosis sera against .alpha.-ketoglutarate dehydrogenase complex-E2 inhibited only .alpha.-ketoglutarate dehydrogenase complex activity but did not alter enzyme activity of either pyruvate dehydrogenase complex or branched chain .alpha.-ketoacid dehydrogenase complex. Finally, .alpha.-ketoglutarate dehydrogenase complex-E2 specific affinity-purified antisera did not react on immunoblot with any component enzymes of pyruvate dehydrogenase complex or branched chain .alpha.ketoacid dehydrogenase complex. These data demonstrate that the E2 component of .alpha.-ketoglutarate dehydrogenase complex is recognized by a distinct population of autoantibodies separate from autoantibodies that recognize pyruvate dehydrogenase complex-E2 or branched chain .alpha.ketoacid dehydrogenase complex-E2. Our data further suggest that these autoantibodies are directed toward a fnctional domain of this enzyme.

- ANSWER 19 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

 A new method using hydrophobic interaction chromatography on phenyl-Sepharose was developed to purify branched chain .alpha.
 ketoacid dehydrogenase complex from commercially available frozen rat liver. Yields of greater than 50% were routinely achieved. The purified enzyme, composed of E1.alpha.,

 E1.beta., and E2 subunits, appeared homogeneous on sodium dodecyl sulfate-polyacrylamide gel electrophoresis and contained endogenous kinase activity for phosphorylation and inactivation of the complex.
- ANSWER 20 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. L7 Limited proteolysis has been used to probe the subunit structure (Mr = AΒ 52,000) of the dihydrolipoyl transacylase (E2) component of the branched-chain .alpha.-keto acid dehydrogenase complex from bovine liver. Digestion of the complex at 0.degree. C with a low concentration of trypsin produces an inner E2 core that retains the activity for the transacylation reaction and is completely dissociated from the decarboxylase (E1) component. The trypsinized E2 maintains the highly assembled structure and migrates faster than the native **E2** in the Sepharose 4B column. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis shows that the inner E2 core consists of two lipoate-free tryptic fragments, i.e. fragment A and fragment B with Mr = 26,000 and 22,000, respectively. Both fragments apparently fail to bind the E1 component. Fragment A is converted into fragment B by increasing trypsin concentrations. Fragment B is a stable limit polypeptide containing the intersubunit-binding sites for **E2**. The assemblage of fragment B confers the cubelike appearance of the inner E2 core in electron micrographs. Activity measurements indicate that the larger fragment A, but not fragment B, possesses transacylation activity. It is likely that a critical portion of the active site is present in the 4,000-dalton fragment that is lost during the conversion of fragment A to B.
- L7 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2002 ACS
- AB Unavailable
- L7 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2002 ACS
- The present invention relates to DNA sequences that encode the branched-chain alpha-ketoacid dehydrogenase complex of an organism belonging to the genus Streptomyces and to polypeptides produced by the expression of such sequences. It also relates to methods of enhancing the prodn. of natural avermectin and of producing avermectin through fermn. The bkd genes for A. avermitilis E1.alpha., E1.beta., and E2 subunits were

cloned, sequenced, and expressed in E. coli.

7 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2002 ACS

Levels of expression of two subunits of the liver branched-chain .alpha.-AΒ ketoacid dehydrogenase complex in response to extremes of dietary protein intake (50% vs. 0% protein diet) were detd. by quant. immunoblotting. Dietary protein deficiency decreased the amt. of E1.alpha. protein to a greater extent than E2 protein. The ratio of E1.alpha. to E2 was below 1 in the liver of animals starved for protein and above 1 in the liver of animals fed the high-protein diet. Supplementation of the 0% protein diet with 5% leucine (but not 5% valine) had the same effect as the 50% protein diet. The extremes of dietary protein also resulted in a divergent pattern of expression of the mRNAs for the subunits of the complex. The E1 .beta. message showed the expected corollary of being greater in the liver of the high-protein-fed rats than the no-protein-fed rats. In contrast, the **E2** message was not affected by the two extremes of dietary protein and the E1.alpha. message was greater in the liver of the no-protein-fed rats than the high-protein-fed rats. Thus, coordinate regulation of gene expression of the subunits of the complex does not occur in response to dietary protein. Posttranscriptional regulatory mechanisms most likely det. the amt. of the complex and the ratio of its subunits. The decrease in E1.alpha./E2 protein ratio that occurs in dietary protein deficiency may increase sensitivity of the complex to phosphorylation-mediated inhibition by branched-chain .alpha.-ketoacid dehydrogenase kinase.

ANSWER 24 OF 24 CAPLUS COPYRIGHT 2002 ACS L7 Ten independent lipoamide dehydrogenase mutants (lpd) of .EPSILON.. coli AΒ were isolated by selecting strains which required supplements of acetate plus succinate for best growth on glucose. They did not grow on unsupplemented medium (except anaerobically) nor did they grow with single supplements of acetate or lipoate, but they responded slowly to lysine plus methionine or succinate. Bacteria-free exts. of the mutants had 1-10% of parental lipoamide dehydrogenase activity and no activity for the pyruvate and .varies.-ketoglutarate dehydrogenase complexes was detected. Evidence that the mutants contained the dehydrogenase (E1) and transacylase (E2) components of the complexes and were deficient only in the lipoamide dehydrogenase (E3) components was obtained from studies with mixts. contg. lpd mutant exts. and either exts. of other mutants having defined lesions or purified lipoamide dehydrogenase, e.g., overall pyruvate dehydrogenase complex was reconstituted with exts. of ace.EPSILON. and F mutants and the .varies.-ketoglutarate complex was similarly reconstituted with suc.ALPHA. and .BETA. exts. Furthermore, both complexes were restored by adding ext. of an ace.EPSILON., suc .ALPHA. double-amber mutants (which lacks both types of E1 and E2 component but has 30% of parental lipoamide dehydrogenase activity) or with purified bacterial and mammalian lipoamide dehydrogenases. The bacterial enzymes were several times more efficient than the mammalian enzyme for restoring pyruvate dehydrogenase complex activity. Genetic studies indicated that the wild-type phenotype was restored by single reversion or transduction events and confirmed that the mutants were deficient only in lipoamide dehydrogenase. The mutant phenotype was introduced into a recipient stain by cotransduction with leu+. This indicates that there is a lipoamide dehydrogenase gene in the leu region of the .EPSILON.. coli linkage map and strongly supports the view that the E3 components of both .varies.-ketoacid dehydrogenase complexes are specified by a single lipoamide dehydrogenase gene (lpd).

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- CS University of Tokyo, Tokyo, Japan.
- AV DNAL (381 J824)
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 Publisher: Bethesda, Md.: American Society for Biochemistry and Molecular Biology.
 - CODEN: JBCHA3; ISSN: 0021-9258
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- CY Maryland; United States
- DT Article
- FS U.S. Imprints not USDA, Experiment or Extension
- LA English
- L7 ANSWER 2 OF 24 AGRICOLA
- AN 94:48646 AGRICOLA
- DN IND20400875
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- AU Zhao, Y.; Popov, K.M.; Shimomura, Y.; Kedishvili, N.Y.; Jaskiewicz, J.; Kuntz, M.J.; Kain, J.; Zhang, B.; Harris, R.A.
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- DN PREV200200148454
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- CS (1) Department of Bioscience, Nagoya Institute of Technology, Nagoya, 466-8555: shimo@ks.kyy.nitech.ac.jp Japan
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- LA English
- L7 ANSWER 4 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
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- TI Gene preference in maple syrup urine disease.
- AU Nellis, Mary M.; Danner, Dean J. (1)
- CS (1) Department of Genetics, Emory University School of Medicine, 1462 Clifton Road, Room 446, Atlanta, GA, 30322: ddanner@emory.edu USA
- SO American Journal of Human Genetics, (January, 2001) Vol. 68, No. 1, pp. 232-237. print.

ISSN: 0002-9297.

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- LA English
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- CS (1) Department of Biochemistry, Kagoshima Women's Junior College, Kagoshima, 890-8565 Japan
- SO Vitamins (Kyoto), (August, 2000) Vol. 74, No. 8, pp. 411-422. print. ISSN: 0006-386X.
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- CS (1) Department of Pediatrics, University of Maryland School of Medicine, 900 Caton Avenue, Baltimore, MD, 21229 USA
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 ISSN: 0264-6021.
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- LA English
- SL English
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- CS (1) Dep. Biochem., Univ. Tex. Southwestern Med. Cent., Dallas, TX USA
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- CS Kansas State Univ., Manhattan, KS 66506 USA
- SO FASEB Journal, (1995) Vol. 9, No. 6, pp. A1288.

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- DT Conference
- LA English
- L7 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
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- DN PREV199497402512
- TI Site-directed mutagenesis of phosphorylation sites of the branched chain alpha-ketoacid dehydrogenase complex.

- AU Zhao, Yu; Hawes, John; Popov, Kirill M.; Jaskiewicz, Jerzy; Shimomura, Yoshiharu; Crabb, David W.; Harris, Robert A. (1)
- CS (1) Dep. Biochem. Mol. Biol., Indiana Univ. Sch. Med., 635 Barnhill Dr., Indianapolis, IN 46202-5122 USA
- SO Journal of Biological Chemistry, (1994) Vol. 269, No. 28, pp. 18583-18587. ISSN: 0021-9258.
- DT Article
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- L7 ANSWER 10 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 1994:126808 BIOSIS
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- AU Chinsky, Jeffrey M. (1); Bohlen, Lizabeth M.; Costeas, Paul A.
- CS (1) Div. Human Genetics, Univ. Maryland Sch. Med., 655 West Baltimore St., 11-037, Baltimore, MD 21201 USA
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- CS DEP. BIOCHEM., UNIV. TEXAS SOUTHWESTN MED. CENTER 5323 HARRY HINES BLVD., DALLAS, TEX. 75235-9038.
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- AN 1991:112923 BIOSIS
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- TI PHYLOGENETIC COMPARISONS OF THE BRANCHED-CHAIN ALPHA KETOACID DEHYDROGENASE COMPLEX.
- AU EISENSTEIN R S; MILLER R H; HOGANSON G; HARPER A E
- CS DEP. BIOCHEMISTRY, COLLEGE AGRICULTURAL AND LIFE SCIENCES, UNIVERSITY WISCONSIN-MADISON, MADISON, WIS. 53706, USA.
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- CS WADSWORTH CENT. LAB. RES., NEW YORK STATE DEP. HEALTH, P.O. BOX 509, ALBANY, N.Y. 12201-0509.
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- CODEN: PIXXD2
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 LA English
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- SO Arch. Biochem. Biophys. (1994), 308(1), 446-53 CODEN: ABBIA4; ISSN: 0003-9861
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- AN 1994:389512 BIOSIS
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- TI Site-directed mutagenesis of phosphorylation sites of the branched chain alpha-ketoacid dehydrogenase complex.
- AU Zhao, Yu; Hawes, John; Popov, Kirill M.; Jaskiewicz, Jerzy; Shimomura, Yoshiharu; Crabb, David W.; Harris, Robert A. (1)
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- L7 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 1991:112923 BIOSIS
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- TI PHYLOGENETIC COMPARISONS OF THE BRANCHED-CHAIN ALPHA KETOACID DEHYDROGENASE COMPLEX.
- AU EISENSTEIN R S; MILLER R H; HOGANSON G; HARPER A E
- CS DEP. BIOCHEMISTRY, COLLEGE AGRICULTURAL AND LIFE SCIENCES, UNIVERSITY WISCONSIN-MADISON, MADISON, WIS. 53706, USA.
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- L7 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2002 ACS
- AN 1995:634550 CAPLUS
- DN 123:27224
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 dehydrogenase complex from Streptomyces and manufacture
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- IN Denoya, Claudio D.
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L7 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

Regulation of the branched chain alpha-ketoacid dehydrogenase complex, the rate-limiting enzyme of branched chain amino acid catabolism, involves phosphorylation of 2 amino acid residues (site 1, serine 293; site 2, serine 303). To directly assess the roles played by these sites, site-directed mutagenesis was used to convert these serines to glutamates and/or alanines. Functional E1 heterotetramers were expressed in Escherichia coli carrying genes for E1-alpha and E1-beta under control of separate T7 promoters in a dicistronic vector. Mutation of phosphorylation site 1 serine to glutamate inactivated E1 activity, i.e., mimicked the effect of phosphorylation of site 1. Replacement of the site 1 serine with alanine greatly increased K-m for the alpha-ketoacid substrate but had no effect on maximum velocity. The site 1 serine to alanine mutant was phosphorylated at site 2, but phosphorylation had no effect upon enzyme activity. Mutation of site 2 serine to either glutamate or alanine also had no effect upon enzyme activity, but phosphorylation of these proteins at site 1 inhibited enzyme activity. E1 mutated to change both phosphorylation site serines to glutamates was without enzyme activity. The binding affinity of E1 to the E2 core was not affected by mutation of the phosphorylation sites to glutamates, suggesting no gross perturbation of the association of E1 with the E2 core. The results provide direct evidence that a negative charge at phosphorylation site 1 is responsible for kinase-mediated inactivation of E1. Site 2 is silent with respect to regulation of activity by phosphorylation.

Regulation of the branched chain alpha-ketoacid dehydrogenase complex, the rate-limiting enzyme of branched chain amino acid catabolism, involves phosphorylation of 2 amino acid residues (site 1, serine 293; site 2, serine 303). To directly assess the roles played by these sites, site-directed mutagenesis was used to convert these serines to glutamates and/or alanines. Functional E1 heterotetramers were expressed in Escherichia coli carrying genes for E1-alpha and E1-beta under control of separate T7 promoters in a dicistronic vector. Mutation of phosphorylation site 1 serine to glutamate inactivated E1 activity, i.e., mimicked the effect of phosphorylation of site 1. Replacement of the site 1 serine with alanine greatly increased K-m for the alpha-ketoacid substrate but had no effect on maximum velocity. The site 1 serine to alanine mutant was phosphorylated at site 2, but phosphorylation had no effect upon enzyme activity. Mutation of site 2 serine to either glutamate or alanine also had no effect upon enzyme activity, but phosphorylation of these proteins at site 1 inhibited enzyme activity. **E1** mutated to change both phosphorylation site serines to glutamates was without enzyme activity. The binding affinity of E1 to the E2 core was not affected by mutation of the phosphorylation sites to glutamates, suggesting no gross perturbation of the association of E1 with the E2 core. The results provide direct evidence that a negative charge at phosphorylation site 1 is responsible for kinase-mediated inactivation of E1. Site 2 is silent with respect to regulation of activity by phosphorylation.

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ANSWER 16 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

Antibodies against the Elb and E2b components of bovine branched-chain .alpha.-ketoacid (BCKA) dehydrogenase (BCKAD) complex completely inhibited BCKA oxidation in mammalian and avian mitochondria. BCKA oxidation by salmonid mitochondria was less affected and the enzyme from Pseudomonas putida was unaffected. In rodents, anti-Elb E2b IgG inhibited oxidation of all three BCKA in a similar dose-dependent manner; oxidation of .alpha.-ketobutyrate and .alpha.-keto-.gamma.-methiolbutyrate was also partially inhibited. Except for the salmonid BCKAD, a similar Mr for the E2b and E1b .alpha. proteins was observed in these species. After digestion with V-8 protease similar immunoreactive peptides were observed for the human and rodent complex.

Antibodies against the **E1b** and **E2b** components of bovine branched-chain .alpha.-ketoacid (BCKA) dehydrogenase (BCKAD) complex completely inhibited BCKA oxidation in mammalian and avian mitochondria. BCKA oxidation by salmonid mitochondria was less affected and the enzyme from Pseudomonas putida was unaffected. In rodents, anti-**E1b E2b** IgG inhibited oxidation of all three BCKA in a similar dose-dependent manner; oxidation of .alpha.-ketobutyrate and .alpha.-keto-.gamma.-methiolbutyrate was also partially inhibited. Except for the salmonid BCKAD, a similar Mr for the **E2b** and **E1b** .alpha. proteins was observed in these species. After digestion with V-8 protease similar immunoreactive peptides were observed for the human and rodent complex.

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L7 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2002 ACS

The present invention relates to DNA sequences that encode the branched-chain alpha-ketoacid dehydrogenase complex of an organism belonging to the genus Streptomyces and to polypeptides produced by the expression of such sequences. It also

relates to methods of enhancing the prodn. of natural avermectin and of producing avermectin through fermn.. The bkd genes for A. avermitilis E1.alpha., E1.beta., and E2 subunits were cloned, sequenced, and expressed in E. coli.

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